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EXAMINER	
HIRIYANNA, KELAGINAMANE T	
ART UNIT	PAPER NUMBER
1633	
MAIL DATE	DELIVERY MODE
10/13/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/594,177	EHLICH, ANDREAS	
	Examiner	Art Unit	
	KELAGINAMANE HIRIYANNA	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 July 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-47 and 49-53* is/are pending in the application.

4a) Of the above claim(s) *10,13-47 and 49-53* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9,11 and 12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *06/08; 09/09; 07/10*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's response to 07/26/2010 is entered.

Applicants are required to follow Amendment Practice under revised 37 CFR §1.121. The fax phone numbers for the organization where this application or proceeding is assigned is ***571-273-8300.***

Election/Restrictions

Applicant's election with traverse of Group I (Claims 1-9, 11 and 12 in the reply filed on 07/26/2010 is acknowledged. Applicant traverses on the grounds that the inventions as restricted relate to a single inventive concept under PCT Rule 13.1 and further argues that at least Group I and II satisfy the unity of invention requirement, since there a common technical feature. Applicant first should note that the restriction was based on PCT rule that allows restriction on the basis that a claimed special technical feature that links the invention does not make a contribution over prior art. The cited references in Restriction/Election for example Goldspink et al (US2003/008836) clearly anticipates the invention as it encompasses all the elements of the base claim the invention is obvious over Wobus & Benkel and have further been cited below for a 35USC102/103 rejections of instant invention. Hence the restriction as indicated in the office action of 06/23/2010 is proper and made final. Applicant's election of species without traverse has been acknowledged.

Claims 48 and 54 were previously canceled.

Claims 10, 13-47 and 49-53 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Election was made **with t**raverse in the reply filed on 6/4/10.

Claims 1-9 and 11, and 12 are considered with respect to the elected invention and are under examination.

Specification

The specification is objected-to.

The specification fails to list the current status, the PCT filing and the priority documents from which it is derived on the first paragraph. Applicant is required to correct this.

Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

"The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same, and shall set forth the best mode contemplated by the inventor of carrying out his invention."

Claims 1-9 & 11-12 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The scope of invention as claimed encompasses monitoring differentiation of cells containing any recombinant nucleic acid molecule comprising a reporter gene encoding a secreted product and by further limitations claimed said reporter gene could be with or without an operably linked regulatory or tissue specific sequences or a secretory leader sequence. The scope the invention further encompasses embryoid bodies as well as tissue like aggregates or cell aggregates which are not embryoid bodies.

The specification at best teaches only teaches the expression of a gene encoding a secretory product SEAP under the control of a promoter of a mouse alpha-myosin gene and does not tech any other reporter gene under the control of any other promoter or regulatory sequence or a reporter gene without a regulatory sequence that is being used for monitoring differentiation of any cell.. The art at the time of invention only teaches expression of reporter genes under at least one regulatory/promoter sequences in order obtain an expression. Further regarding broad claims to any aggregated cell structures, the specification only teaches cells which form embryoid bodies and does not teach any other cell aggregates or tissue aggregates.

Applicant is referred to the guidelines for ***Written Description Requirement*** published January 5, 2001 in the Federal Register, Vol.66, No.4, pp.1099-1110 (see <http://www.uspto.gov>). The disclosure of a single species is rarely, if ever, sufficient to describe a broad genus, particularly when the specification fails to describe the features of that genus, even in passing. In analyzing whether the written description requirement is met for the genus claim, it is first determined whether a representative number of species have been described by their complete structure. Next, it is determined whether a representative number of species have been sufficiently described by other relevant identifying characteristics.

Since the specification fails to disclose other regulatory sequences or an expression construct with no regulatory sequence for driving the specific expression of reporter gene in a differentiating cells, it is not possible to envision the broadly claimed expression strategies used for the expression of secreted reporter gene product in a differentiating cell. Still further the specification only teaches cells that form embryoid bodies and does not show the possession of any other cell aggregate forms. Still further the specification does show the possession of a secreted reporter protein that does not require a leader or secretory signal sequence. One cannot describe what one has not conceived. Therefore, the lack of disclosure in the specification is not deemed sufficient to reasonably convey to one skilled in the art that the applicants were in possessions of the huge genera recited in the claims at the time the application was filed. Furthermore the possession may be shown by actual reduction to practice, clear depiction of the invention in a detailed drawing, or by describing the invention with *sufficient relevant identifying characteristics* (as it relates to the claimed invention as a whole) such that a person skilled in the art would recognize that the inventor had possession of the claimed invention. Accordingly one of skill in the art would conclude that applicant was not in possession of the claimed genus because a description of a single member of this genus would not be representative of claimed genus of compounds and is insufficient to support the claim in its present scope.

Claims 1-9 & 11-12 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabled for a method of monitoring differentiation of stem cell into specific cell lineage by measuring the amount of secreted activity of a reporter gene product by the differentiated cell wherein said gene expressed in the differentiating cell under the control of a operatively linked tissue specific regulator/promoter specific to said differentiating cells is not enabled for any reporter gene in any recombinant nucleic acid and further is not enabling for reporter gene encoding a product without an operatively linked signal sequence or a leader sequence. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The scope of invention as claimed encompasses monitoring differentiation of cells containing any recombinant nucleic acid molecule comprising a reporter gene encoding a secreted product and by further limitations claimed said reporter gene could be with or without an operatively linked regulatory or tissue specific sequences or a secretory leader sequence.

The specification at best teaches only teaches the expression of a gene encoding a secreted reporter gene product SEAP under the control of a promoter of a mouse alpha-myosin gene and does not tech any other reporter gene under the control of any other promoter or regulatory sequence or a reporter gene without a regulatory sequence that is being used for monitoring differentiation of any cell.. The art at the time of invention only teaches expression of reporter genes under at least one regulatory sequence or a promoter in order obtain an expression of said reporter gene in cell type specific manner..

Since the specification fails to disclose enabled examples of gene constructs that encompass the scope and breadth of instant claims, it would be undue experimentation to one of skill in the art to determine any reporter gene with or without an operatively linked signal sequence and cell type specific regulatory/promoter sequence could equivalently be used in monitoring differentiation of a stem cell into a specific cell type. The applicant's disclosure does not enable one skilled in the art to practice the invention as claimed without further undue amount of experimentation. At issue, under the enablement requirement of 35 U.S.C. 1 12, first paragraph is whether, given the Wands-factors, the

experimentation was undue or unreasonable under the circumstances. "Experimentation must not require ingenuity beyond that to be expected of one of ordinary skill in the art." See Fields v. Conover, 443 F.2d 1386, 170 USPQ 276 (CCPA 1970).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-8 and 11 are rejected under 102(b) as being anticipated by Goldspink et al., (US 2003/0008836 A1).

The above claims are drawn to a method of monitoring cell differentiation comprising steps of culturing cell capable of differentiating wherein said cells contain at least one recombinant nucleic acid molecule comprising a reporter gene encoding a product that is secreted upon cell differentiation or maintaining a non human animal comprising said cells under conditions allowing differentiation and determining the amount of activity of the reporter gene product in the culture medium or in the body fluid..

Goldspink clearly teaches a method of detecting myoblast differentiation by transfecting recombinant nucleic acid molecules encoding a human alpha-gal reporter gene under the control of promoter comprising MLC1/3 enhancer to undifferentiated myoblasts wherein the reporter gene was expressed and secreted from differentiated muscle cell in vitro culture (entire article; abstract; specifically paragraphs (0052-0059). Thus the rejected claims are within the scope of the Goldspinks's disclosure.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-9 and 11 & 12 are rejected under 35 USC 103 (a) as being unpatentable over Wobus et al (1997 J. Mol. Cell. cardiol. 29:1525-1539) in view of Benkel et al (WO 98/49320)

The above claims are drawn to a method of monitoring cell differentiation comprising steps of culturing cell capable of differentiating wherein said cells contain at least one recombinant nucleic acid molecule comprising a reporter gene encoding a product that is secreted upon cell differentiation or maintaining a non human animal comprising said cells under conditions allowing differentiation and determining the amount of activity of the reporter gene product in the culture medium or in the body fluid..

Regarding claims Wobus teaches a method of monitoring cell differentiation of embryonic stem cells into cardiomyocytes by transfecting the stem cells with pGNA/MLC2 containing the lacZ reporter gene and cultivating as embryoid bodies and plating them followed by a treatment with retinoic aid to induce them to differentiate (entire article; abstract) and express lacZ gene or its Beta-galactosidase product. A quantitative and qualitative monitoring of differentiation of ES cells to cardiomycytes was carried out by assaying for the expression of Beta-galactosidase enzyme (p.1527-1529) in the cells. Wobus however, does not teach that the reporter gene product was secreted in to the culture medium.

WO 98/49320 teaches the advantages of using a reporter gene whose expression product is secretable for monitoring mammalian gene regulations (entire article; abstract). WO 98/49320 teaches that there are several secretable reporter systems that including a secreted alkaline phsophatase (SEAP), alpha-amylase, hGH etc (p.1-2).

Thus it would have been obvious for one of ordinary skill in the art to substitute lacZ gene in the reporter construct of Wobus for a reporter gene that codes for a secreted enzyme as taught by WO 98/49320 and follow the differentiation of stem cells to specific tissue types or cell types. One of ordinary skill in the art would have been motivated to make and use of an assayable secreted reporter for monitoring a gene regulation as it is

less invasive and avoids lysis of the cells. One of ordinary skill in the art would have reasonable expectation of success making using secretable reporter assay for identifying the differentiated cells as the art teaches making and using of gene constructs and assay systems for said assay is routine in the art. Thus, the claimed invention was *prima facie* obvious.

Double Patenting Warning

Applicant is advised that should claim 1 be found allowable, claim 3 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k). Claim 3 requires the cells be derived from stem cells, such depends from Claim 1, directly, which requires that a differentiating cell and it is inherent all differentiating cells are derived from stem cells, therefore, despite a slight difference in wording, Claim 3 is a substantial duplicate of Claim 1.

Conclusion:

No claim allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner *Kelaginamane Hiriyanna Ph.D.,* whose telephone number is **(571) 272-3307**. The examiner can normally be reached Monday through Thursday from 9 AM-7PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, *Joseph Woitach Ph.D.,* may be reached at **(571) 272-0739.** The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private

PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). When calling please have your application serial number or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. For all other customer support, please call the USPTO call center (UCC) at (800) 786-9199.

/Robert M Kelly/

Primary Examiner, Art Unit 1633